REMARKS

The Commissioner is authorized to charge any additional fees, including any extension fees, which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-62629/RFT/RMS).

The applicants acknowledge the withdrawal of the previous rejection under 35 U.S.C. §103 over Wagner et al. or Ryser et al. (A & B).

Claims 1-22 are in the case.

Claims 1-4, 6-10, 12-13, 16 and 22 are provisionally rejected under 35 U.S.C. §101 as claiming the same invention as claims 1-8, 12 and 21-23 of copending application U.S.S.N. 08/321,552.

The applicants respectfully request that the rejection be held in abeyance until otherwise allowable subject matter is found.

Claims 5, 11, 14-15, and 17-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentably over claims 9-11, 24-27, and 35 U.S.C. §-38 of copending application U.S.S.N. 08/321,552.

The applicants respectfully request that the rejection be held in abeyance until otherwise allowable subject matter is found.

Claims 1-22 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wagner et al., in view of Kornguth et al.

The present invention teaches compositions and methods using delivery vehicles which can specifically deliver physiological agents such as contrast agents and therapeutic agents. The delivery vehicles generally comprise four elements: (1) a first polymeric molecule having a net positive or negative charge; (2) a second polymeric molecule having a net charge opposite to the first polymeric molecule; (3) a cell targeting moiety attached to the second polymeric

molecule; and (4) a physiological agent attached to either the first or second polymeric molecule (or a third polymeric molecule similar to the second polymeric molecule). The physiological agent can be a therapeutic agent, such as a drug, hormone, enzyme, protein or peptide, anti-cancer agent, etc., or a contrast agent, such as magnetic resonance imaging contrast agents, radioisotope contrast agents, gamma emitter contrast agents, positron emitter contrast agents, beta emitter contrast agents and optical contrast agents, including fluorescent contrast agents. The applicants submit that none of the prior art references, taken alone or in combination, teaches or suggests the present invention.

Wagner et al. is directed to high-efficiency nucleic acid delivery systems, i.e. ways of getting nucleic acids into cells. Wagner et al. teaches compositions and methods using complexes with three components: (1) a DNA molecule; (2) a polycation; and (3) transferrin molecules. It is the delivery of the nucleic acid which is important to Wagner et al.; Wagner et al. does not teach or suggest the addition of a physiological agent such as a therapeutic agent or contrast agent.

Kornguth et al. is directed to methods and compositions for imaging tumors which have a net positive charge and thus will preferentially bind to tumors which have a net negative charge. Kornguth et al. teaches the use of polylysine linked to a metal chelator, DTPA, (a "linking molecule") which then will bind a metal which can be used either for imaging (i.e. paramagnetic metals such as Gd or Mn) or as a chemotherapeutic agent (i.e. radioisotopes such as gamma or beta emitters). Kornguth et al. does not teach or suggest the use of a second polymer, nor does Kornguth teach or suggest the use of a cell targeting moiety.

As stated in M.P.E.P. §2142, three basic criteria must be met to establish a prima facie case of obviousness. First of all, there must be some

motivation to practice the invention. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all of the claim limitations.

Neither Wagner et al. nor Kornguth et al., taken alone or in combination, provide motivation to make compositions comprising four components:(1) a first polymeric molecule having a net positive or negative charge; (2) a second polymeric molecule having a net charge opposite to the first polymeric molecule; (3) a cell targeting moiety attached to the second polymeric molecule; and (4) a physiological agent attached to either the first or second polymeric molecule (or a third polymeric molecule similar to the second polymeric molecule).

Wagner et al. does not teach or suggest the addition of a physiological agent such as a therapeutic agent or contrast agent; Wagner is solely interested in nucleic acid delivery and has no interest in either imaging or therapeutic agent delivery.

Kornguth et al. capitalizes on charge differences between tumor cells and other tissues to effect targeting; thus, components which would decrease the net positive charge of the Kornguth et al. compositions, such as the addition of a polyanion as disclosed in the present invention, would be disfavored. As outlined in M.P.E.P. §2143.01:

> If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.

See In re Gordon, 221 USPQ 1125 (Fed. Cir. 1984). Thus, the combination is improper and the rejection should be withdrawn.

In addition, Kornguth et al. does not teach or suggest the use of cell targeting moieties. Kornguth et al. relies on charge differences to effect

targeting. In fact, adding the transferrin protein from Wagner to the Kornguth compositions could result in a loss of targeting in Kornguth, since, as pointed out in Wagner, all actively metabolizing cells require iron that is taken up via a transferrin mechanism (see first sentence after the abstract). As argued above, this might render the Kornguth et al. compositions unsuitable for their intended purpose, and is therefore impermissible.

Accordingly, the applicants submit that the neither Wagner nor Kornguth, taken alone or in combination, provides the requisite motivation to practice the invention, and thus the rejection is improper.

Even assuming, arguendo, that there is motivation, there is not a reasonable expectation of success. As outlined above, the addition of a polyanion to Kornguth could result in a loss of targeting to tumor cells, due to a loss of net positive charge that forms the basis of the targeting in Kornguth. Similarly, the addition of transferrin, which is taken up by actively metabolizing cells, could also potentially result in a loss of specific tumor targeting.

Finally, as outlined in M.P.E.P. §2142, the initial burden is on the Examiner to provide some suggestion of the desirability of doing what the inventor has done. This the Examiner has not done.

Accordingly, the applicants submit that the references, taken alone or in combination, do not render the claimed invention, taken as a whole at the time the invention was made, obvious to a person skilled in the art, and the rejection should be withdrawn.

The applicant maintains that the claims are now in condition for allowance and an early notification of such is solicited.

Respectfully submitted,

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